

Received 16 November 2004

10/524619

- 82 -

DT05 Rec'd PCT/PTO 09 FEB 2005

CLAIMS

1. An isolated nucleic acid molecule comprising a sequence of nucleotides encoding or complementary to a sequence encoding a mammalian transcription factor comprising an amino acid sequence selected from SEQ ID NO:8 (human SOM), SEQ ID NO:16 (murine SOM) and an amino acid sequence having at least 75% identity to SEQ ID NO:8 or SEQ ID NO:16 after optimal alignment.
2. The isolated nucleic acid molecule of claim 1 wherein the mammalian transcription factor is encoded by a nucleotide sequence having at least 75% identity after optimal alignment to one or more of SEQ ID NO:7 (human *som*) or SEQ ID NO:15 (murine *som*) or a nucleotide sequence capable of hybridizing to SEQ ID NO:7 or 15 or a complementary form thereof under stringency conditions.
3. The isolated nucleic acid molecule of claim 1 or 2 encoding a polypeptide comprising an amino acid sequence selected from SEQ ID NO:8 and SEQ ID NO:16.
4. The isolated nucleic acid molecule of claim 1 comprising a nucleotide sequence selected from SEQ ID NO:7 and SEQ ID NO:15.
5. An isolated nucleic acid molecule comprising the nucleotide sequence set forth in SEQ ID NO: 7.
6. An isolated nucleic acid molecule comprising the nucleotide sequence set forth in SEQ ID NO: 15.

7. Use of an isolated nucleic acid molecule comprising a sequence of nucleotides encoding or complementary to a sequence encoding a mammalian homolog of *Drosophila grh* wherein the nucleic acid molecule encodes a transcription factor selected from human SEQ ID NO: 2 (MGR p49), SEQ ID NO: 4 (human MGR p70), SEQ ID NO: 6 (human BOM), SEQ ID NO: 7 (human SOM), SEQ ID NO: 10 (murine MGR p61), SEQ ID NO: 12 (murine MGR p70), SEQ ID NO: 14 (murine BOM) and SEQ ID NO: 16 (murine SOM) or transcription factor having at least 65% identity to SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14 or SEQ ID NO: 16 after optimal alignment in the manufacture of a medicament for the treatment of spinabifida or other physiological or genetic disorder.
8. Use of claim 7 wherein the mammalian homolog comprises a nucleotide sequence having at least 75% identity after optimal alignment to one or more of SEQ ID NO: 17, SEQ ID NO: 34, SEQ ID NO: 36 and SEQ ID NO: 38 or comprises a nucleotide sequence capable of hybridizing to SEQ ID NO: 17, SEQ ID NO: 34, SEQ ID NO: 36 and/or SEQ ID NO: 38 or a complementary form thereof under stringency conditions.
9. Use of claim 7 wherein the nucleic acid molecule comprises a sequence of nucleotides encoding a polypeptide having transcription factor activity and comprising an amino acid sequence selected from SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14 and SEQ ID NO: 16.
10. Use of claim 7 wherein the nucleic acid molecule comprises a nucleotide sequence selected from SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 11, SEQ ID NO: 13 and SEQ ID NO: 15.

11. A method of identifying a nucleotide sequence likely to encode an M-GRH transcription factor, said method comprising interrogating a mammalian genome database conceptually translated into different reading frames with an amino acid sequence defining *Drosophila GRH* or any one of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14 and SEQ ID NO:16 and identifying a nucleotide sequence corresponding to an amino acid sequence having at least about 70% similarity to *Drosophila GRH* or to any one of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14 and SEQ ID NO:16 and then determining that the nucleotide sequence exhibits a restricted pattern of expression.
12. Use of an isolated mammalian transcription factor which is a homolog of *Drosophila* grainyhead (GRH) selected from human SEQ ID NO: 2 (MGR p49), SEQ ID NO: 4 (human MGR p70), SEQ ID NO: 6 (human BOM), SEQ ID NO: 8 (human SOM), SEQ ID NO: 10 (murine MGR p61), SEQ ID NO: 12 (murine MGR p70), SEQ ID NO: 14 (murine BOM) and SEQ ID NO: 16 (murine SOM) and a molecule having at least 75% identity to SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14 or SEQ ID NO:16 after optimal alignment in the manufacture of a medicament for the treatment of spinabifida or other physiological or genetic disorder.
13. A method for detecting an embryo with a propensity to develop spinabifida said method comprising contacting said embryo or a cell therefor with agents capable of detecting the level of expression of a transcription factor selected from human SEQ ID NO: 2 (MGR p49), SEQ ID NO: 4 (human MGR p70), SEQ ID NO: 6 (human BOM), SEQ ID NO: 8 (human SOM), SEQ ID NO: 10 (murine MGR p61), SEQ ID NO: 12 (murine MGR p70), SEQ ID NO: 14 (murine BOM) and SEQ ID NO: 16 (murine SOM) and a molecule having at least 75% identity to SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14 or SEQ ID NO:16 after optimal alignment.

- 85 -

14. An animal model comprising a genetically modified animal comprising a nucleotide insertion, deletion, addition and/or substitution in a nucleic acid molecule comprising a nucleotide sequence having at least 75% identity after optimal alignment to one or more of SEQ ID NO:7 (human *som*) or SEQ ID NO:15 (murine *som*) or a nucleotide sequence capable of hybridizing to SEQ ID NO:7 or 15 or a complementary form thereof under stringency conditions of claim 2.
15. A medical assessment system comprising the animal model of claim 14.